BIOCHEMICAL EVALUATION OF SEVERAL AMINO ACIDS AS CANDIDATES FOR SYNAPTIC TRANSMITTERS IN THE MAMMALIAN SPINAL CORD

by

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CHAPTER V

SUMMARY

The early development of the concept of chemical transmission in the nervous system was reviewed. The current ideas of the criteria for the identification of a chemical syanptic transmitter were discussed. The neuroanatomical organization of the spinal cord was presented and discussed in relation to the identification of specific transmitters. This was followed by brief discussions on the excitatory and depressant effects of some amino acids on spinal neurons and on the proposed work in the cat spinal cord. An approach useful in the identification of chemical synaptic transmitters was described.

The surgical procedures used in the preparation of experimental animals, and the removal of tissue were briefly described as well as the extraction and concentration of the amino acids for assay. Very sensitive and specific micromethods for the measurement of the amino acids and related enzymes were developed and are described in detail. The technique of using enzymes to measure substrates was exploited. Fluorometric methods were used for the measurement of glutamate, glutamine, aspartate, GABA, glutaminase, glutamic decarboxylase, GABA transaminase, and aspartate aminotransferase. Spectrophotometric methods were used for the measurement of total free amino acids and glutamine synthetase activity.

The amino acids and related enzyme activities were determined

in four major areas of the cat spinal cord (dorsal white, dorsal gray, ventral gray, and ventral white) and dorsal and ventral roots. The distribution pattern of the amino acids was redetermined in the cord areas after selective interneuronal destruction by aortic occlusion. The distributions of glutamate and aspartate were compared on the homolateral and contralateral sides of the cord after cutting some homolateral dorsal roots. The distribution of glutamate and aspartate were also determined along dorsal and ventral roots between the spinal cord and the dorsal root ganglion.

Following a brief discussion of the metabolism and compartmentalization of amino acids in nerve tissue and the evidence that some amino acids act as synaptic transmitters in various forms of invertebrates, the function of amino acids as synaptic transmitters in the cat spinal cord was discussed. Based on the data presented in this thesis and on the theoretical anatomical (chemical) and physiological behavior of certain transmitters, it was concluded that: (a) glutamate is a prime candidate for the noncholinergic excitatory (sensory) transmitter carried by dorsal root fibers, (b) aspartate is a likely candidate for an excitatory transmitter released by excitatory interneurons. The data indicate that GABA is not likely to be a major inhibitory transmitter in the spinal cord. However, it may be involved with inhibitory transmission from supraspinal centers or with some special type of interneuron located in the periphery of the gray matter.

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